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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,964	12/12/2000	Konstantin Petrukhin	20177YP	8195

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EXAMINER	
SCHNIZER, HOLLY G	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,964	PETRUKHIN ET AL.	
	Examiner	Art Unit	
	Holly Schnizer	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-3,5 and 6* is/are allowed.

6)☒ Claim(s) *14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

In the Reply filed 11-14-03, Applicants confirmed the election of claims 1-6 and 14-17 indicated in the first Office Action (mailed 8/13/03). Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Thus, the requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

The examiner notes that the Amendments filed 11-14-03, 1-12-04, and 6-16-04 have not been entered due to non-compliance with 37 CFR 1.121 (in the case of amendments filed 11-14-03, and 6-16-04 and because the reply was not fully responsive (in the case of amendment filed 1-12-03).

The Amendment filed 4-30-04 has been entered in part. The amendment to the claims has not been entered due to non-compliance with 37 CFR 1.121. However, the amendments to the Specification and Drawing have been entered.

The Amendment and Reply filed 1/12/05 has been entered and considered in this Office Action. Claims 1-3, 5-6, 14-16 are pending and have been examined on the merits in this Office Action.

Drawings—Objection Withdrawn

The objection to the Drawings is withdrawn in light of the Amendment (filed 4-30-04) to the Drawing and the Brief Description of the Drawings.

Objections—Objections Withdrawn

The objections to Claims 1-6 and 14-17 are withdrawn in light of the amendment to the claims.

Rejections Withdrawn

The rejection of Claim 4 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of the claim cancellation.

The rejection of Claims 14-16 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the amendment.

The rejection of Claims 4 and 17 under 35 U.S.C. 102(b) as being anticipated by Adams et al. (Nature (1995) 377(6547 Suppl.) pp. 3-174) is withdrawn in light of the cancellation of these claims.

The rejection of Claims 4 and 17 under 35 U.S.C. 102(b) as being anticipated by the Pharmacia Molecular and Cell Biology Products Catalog (1994) is withdrawn in light of the cancellation of these claims drawn to DNA that hybridizes to or has at least 18 contiguous nucleotides of SEQ ID NOs: 1, 2, 4, or 28.

The rejection of Claim 4 under 35 U.S.C. 102(b) as being anticipated by the Boehringer Mannheim Biochemicals Catalog (1997) is withdrawn in light of the cancellation of these claims drawn to DNA that hybridizes to or has at least 18 contiguous nucleotides of SEQ ID NOs: 1, 2, 4, or 28 .

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining whether a cDNA derived from an individual has a mutation as compared to SEQ ID NO:2 or SEQ ID NO:4 by amplifying the cDNA using the steps of a)-d) of Claim 14 and then comparing the nucleotide sequence of the PCR fragment with the sequence of SEQ ID NO:2 or 4 wherein a sequence of nucleotides that differ from SEQ ID NO: 2 or SEQ ID NO:4 indicates that the cDNA has a mutation as compared to SEQ ID NO:2 or SEQ ID NO:4, does not reasonably provide enablement for a method of diagnosing whether a patient carries a mutation in the CG1CE gene comprising amplifying DNA from a patient using the steps of a)-d) of Claim 14 based on the sequences of SEQ ID NOs: 2 and 4 and then comparing the sequence of the PCR fragment with the sequence of SEQ ID NO:2 or SEQ ID NO:4 wherein a sequence of nucleotides that differ from either SEQ ID NO:1

or SEQ ID NO:2 indicates that the patient carries a mutation in the CG1CE gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d, 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include (1) quantity of experimentation, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The invention involves the discovery of a genomic sequence of CG1CE (SEQ ID NO:1) and two open reading frames resulting from alternative splicing contained within 11 exons (SEQ ID NO:2 and 4). The sequence of SEQ ID NO:2 is the sequence of the 11 exons collectively and the sequence of SEQ ID NO:4 is the result of an alternative splice donor site in exon 7 (see p. 7, lines 10-22). The disclosed sequence of SEQ ID NO:1 (now added to the claim as a reference sequence) contains gaps of unknown sequence. More specifically, there are gaps between exons 1 and 2 and between exons 7 and 8 wherein the sequence of the gaps and the length of the gaps is are unknown (see p. 3, last paragraph). The claim is drawn to a method of diagnosing whether a patient carries a mutation in the CG1CE gene by amplifying a DNA sample from the patient using PCR primers from the cDNA sequences (SEQ ID NOs: 2 and 4)

and comparing the sequence of the PCR products with the sequence of the cDNA's of SEQ ID NO:2 or 4 wherein a conclusion that the patient carries a mutation results from a difference in sequence between the PCR product and either SEQ ID NO:1 (the genomic sequence) or SEQ ID NO:2. However, the sequences that makes up SEQ ID NOS: 2 and 4 are not contiguous in SEQ ID NO:1. For example, exon 2 is nucleotides 3280-3466 and exon 3 is nucleotides 6617-6711 in SEQ ID NO:1, whereas these two regions of sequence are contiguous in SEQ ID NO:1. Thus, using a PCR primer based on the sequence of exon 2 and another based on exon 3 would result in PCR of a larger fragment containing sequences not found in SEQ ID NO:2 or 4 (even though they might be found in SEQ ID NO:1). As a result, the claimed method would always provide a positive result (the patient carries a mutation in the CG1CE gene) when PCR primers are based on sequences from two different exons and the sequence is compared with SEQ ID NOs: 2 or 4. In addition, SEQ ID NO:1 contains gaps in sequence of unknown length. Therefore, if the primers were designed between exons 7 and 8, claimed assay would erroneously indicate a mutation 100% of the time regardless of whether the PCR product was compared with SEQ ID NO:1, 2, or 4. Thus, the claim is not enabled because 1) cDNAs contain only a percentage of the CG1CE gene and therefore basing the diagnosis assay on these sequences would miss mutations in the CG1CE gene that were outside of the PCR product or outside of the cDNA sequence and 2) a large portion of the gene sequence is unknown and therefore comparing the PCR product with SEQ ID NO:1 would miss mutations in the regions of unknown sequence and length.

A method of "*diagnosing whether* a patient carries a mutation" is interpreted to mean a method that provides either a positive (there are mutations) or negative (there are not mutations) result. In the instant case, it does not appear that the claimed method could indicate that a patient had a mutation in the CG1CE gene (a positive result), because of the unknown sequence in SEQ ID NO:1 (results would be ambiguous in the case that the sample is genomic DNA), or that the claimed method could indicate that a patient did not have a mutation in the CG1CE gene, because the cDNAs do not cover the entire gene and mutations might occur outside of the coding regions of the gene (results would be ambiguous regardless of whether the DNA sample was genomic DNA or cDNA).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amendment to Claim 14 recites the limitation "said SEQ ID NO:1" in part (e), line15 of the claim. There is insufficient antecedent basis for this limitation in the claim. Moreover, due to this amendment, the claim is inconsistent because the sequence of the PCR primer is compared to SEQ ID NO:2 or 4 yet the conclusion is based on a comparison of the sequence with SEQ ID NO:1. Claims 15-16 are rejected because

they depend from the rejected claim yet do not correct its deficiencies. Correction is required.

Conclusions

Claims 1-3 and 5-6 are in condition for allowance. Claims 14-16 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-0958. The examiner can normally be reached on Monday through Wednesday from 10 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The Official fax phone number is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703 308-0196.

Holly Schnizer
April 2, 2005

JON WEBER
SUPERVISORY PATENT EXAMINER